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Magnetic resonance imaging of posterior pituitary for evaluation of the neurohypophyseal function in idiopathic and autosomal dominant neurohypophyseal diabetes insipidus

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Abstract. We investigated the role of MR imaging for evaluation of the functional status of the neurohypophyseal system in both idiopathic central diabetes insipidus (DI) and familial autosomal dominant neurohypophyseal DI. The patients and family with DI were analyzed retrospectively for the presence or absence of posterior pituitary gland hyperintense signal on MR images. A total of 19 adult patients with idiopathic central DI, 7 members of a family with autosomal dominant DI and 20 control subjects were included in the study. Diagnosis of idiopathic DI was based on the presence of central DI in the absence of any alteration that is known to be responsible for DI. The patients were studied retrospectively and the morphology and intensity of the posterior lobe by MR imaging was assessed by blinded reading. In all patients with idiopathic central DI and the affected members of the family, the posterior bright signal was absent while the stalk was normal on MR images. In contrast, normal posterior pituitary bright signal and stalk were found in unaffected members of the family and all control subjects. We conclude that MR imaging of the posterior pituitary lobe can be used to evaluate the functional status of the neurohypophyseal system in idiopathic central DI and familial autosomal dominant DI.

Key words: MR imaging – Idiopathic diabetes insipidus – Familial autosomal dominant diabetes insipidus – Neurohypophysis

Introduction

Central diabetes insipidus (CDI) is a disorder of impaired water conservation which results from a deficiency of arginine vasopressin (AVP). Central diabetes insipidus can be classified into three categories: familial, idiopathic and secondary [1]. Familial CDI is a rare hereditary disease usually transmitted as an autosomal dominant trait [2], whereas idiopathic CDI is far more common, comprising 30% of CDI [3].

The standard method of diagnosing central DI is based on water deprivation followed by administration of 1-desamino-8–9 arginine vasopressin (DDAVP) as well as by assessment of the renal response to hypertonic saline infusion. However, recently it has been reported that MR imaging of the neurohypophyseal system can assess the neurohypophyseal reserves of neurosecretory material, and MR can be used as a functional imaging method for the posterior pituitary gland [4]. Nevertheless, conflicting results have been reported about the diagnostic role of MR imaging in central DI or in familial autosomal dominant DI. Some previous studies reported that patients with idiopathic central DI and affected patients with familial autosomal dominant DI had the absent hyperintense signal on MR [5–7], but this was not confirmed by other investigators [8–11]. Moreover, to our knowledge, MR evaluation was only reported on three families with autosomal dominant DI to date [7, 8, 11]. Although the origin of the hyperintense signal of the posterior pituitary lobe is not clear, several studies suggest that neurosecretory granules and/or the intracellular lipid droplets in the posterior pituitary cells (pituicytes) may be its source [12–15].

We have therefore investigated MR imaging in patients with idiopathic DI and in a family with autosomal dominant DI to clarify the role of MR imaging in idiopathic and familial DI.

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Materials and methods

A total of 19 adult patients (18 males and 1 female, median age 21 years, range 20–38 years) with idiopathic central DI and a family with autosomal dominant DI were enrolled in the study. Patients with DI originating from secondary causes, e. g. germinoma, neurosarcoidosis, tuberculosis, neoplasm, distant metastasis, radiotherapy, craniopharyngioma or previous surgery in the pituitary region were excluded. The patients were studied retrospectively, and the morphology and intensity of the signal of the posterior lobe were assessed.

The diagnosis of DI was based on the water deprivation test, and response to exogenous arginine vasopressin [16]. Polyuria and dilute urine of psychogenic or renal origin was excluded. All patients were receiving treatment with DDAVP intranasally. Diagnosis of idiopathic central DI was based on the presence of central DI in the absence of any alteration that is known to be responsible for DI. Clinical characteristics of 19 patients with idiopathic central DI are given in Table 1. All patients had normal anterior pituitary function (either basal or after specific stimuli).

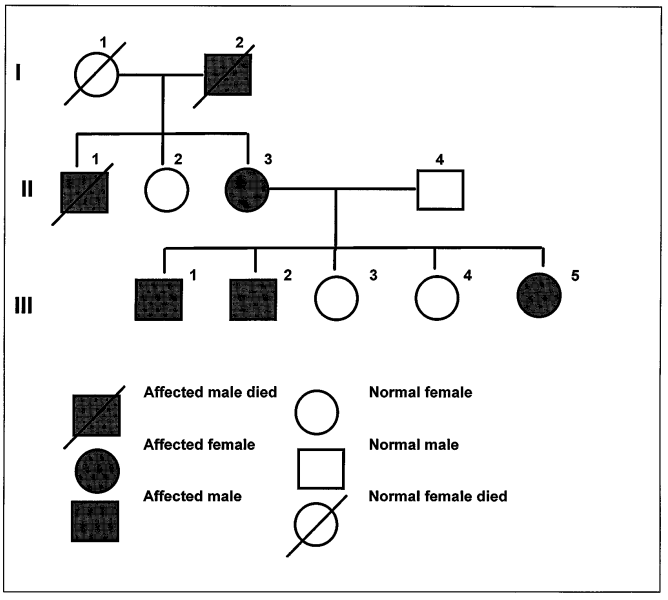


Fig. 1. Pedigree of familial diabetes insipidus (DI)

Family with autosomal dominant DI

The pedigree of the family is shown in Fig. 1.

Mother (II-3)

The mother was 45 years old with a history of increasing polyuria and polydipsia from her childhood. She does not remember exactly when her complaints started. Diabetes insipidus was first diagnosed at approximately 20 years old. Twenty years ago her 24-h urine volume was 15 l/day; presently, it is 7 l/day. Her polyuria has decreased over time. She has responded to intranasal DDAVP therapy with resolution of symptoms. Water deprivation test was consistent with central DI. She has also had hypertension (140/100 mmHg) for 10 years and is using calcium channel blocker (Nitrendipin 10 mg/day). Pituitary MRI showed the absence of hyperintense signal in the posterior pituitary lobe and normal stalk.

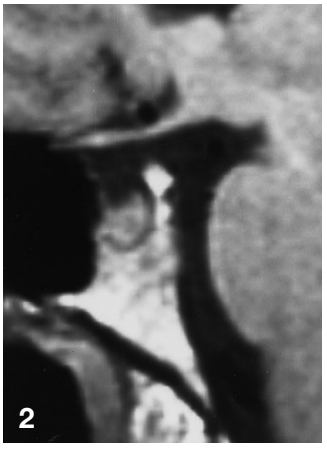
Mother's brother (II-1)

The mother's brother died when he was 49 years old, cause of death not known. He has 5 children (3 girls

Table 1. Characteristics of 19 patients with idiopathic central DI

Case no.[a]	Age (years)	Gender	Amount of 24-h urine without therapy (L)	Known disease duration	Age at diagnosis (years)	MR Findings	
						PP	Stalk
1	20	M	11.5	4	16	Absent	Normal
2	21	M	25	16	5	Absent	Normal
3	21	M	10	17	4	Absent	Normal
4	21	M	7.5	5	16	Absent	Normal
5	20	M	13.5	18	14	Absent	Normal
6	20	M	12	10	20	Absent	Normal
7	21	M	13	4	21	Absent	Normal
8	22	M	7	9	13	Absent	Normal
9	20	M	8.2	18	2	Absent	Normal
10	21	M	10	18	3	Absent	Normal
11	21	M	14.3	3	18	Absent	Normal
12	22	M	7.0	1	21	Absent	Normal
13	20	M	14.5	8	12	Absent	Normal
14	21	M	20	7	14	Absent	Normal
15	40	F	13	36	38	Absent	Normal
16	27	M	11	1	26	Absent	Normal
17	22	M	11	2	20	Absent	Normal
18	21	M	7	20	1	Absent	Normal
19	20	M	11.5	15	5	Absent	Normal

[a] All cases responded to 1-desamino-8-9 arginine vasopressin (DDAVP) therapy



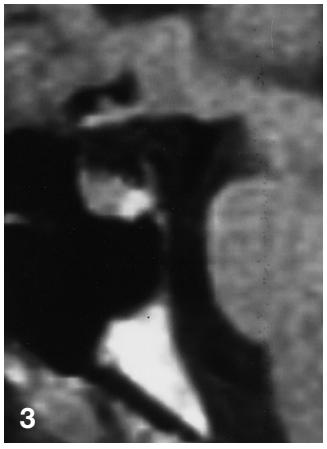


Fig. 2. In a patient with idiopathic central DI , the high signal intensity normally seen in the posterior lobe of the pituitary gland is conspicuously absent on T1-weighted sagittal image

Fig. 3. In an unaffected member of the family (III-4), the posterior lobe of the pituitary gland has normal high signal intensity on T1-weighted sagittal image

and 2 boys). One of the girls is 24 years old and has polyuria; DI has not been established.

Mother's sister (II-2)

The mother's sister is 49 years old and has never had symptoms of DI.

Mother's father (I-2)

The mother's father died at 70 years old. The diagnosis of DI has not been proven, but he is said by his daughter to have also had polyuria.

Mother's daughter (III-5)

The mother's daughter is 19 years old. She had been diagnosed as having diabetes insipidus at the age of 8 months, and now has polyuria of 13 l/day. She has also responded to DDAVP twice a day. A water deprivation test demonstrated a defect in urine-concentrating ability. Pituitary MRI showed the absence of hyperintense signal in the posterior pituitary and normal stalk.

Mother's younger son (III-1)

The mother's younger son is 16 years old. He had been diagnosed as having diabetes insipidus at the age of 3 years. He has also responded to DDAVP. A water deprivation test demonstrated a defect in urine-concentrating ability. His polyuria is 8 l/day. Pituitary MRI showed the absence of hyperintense signal in the posterior pituitary lobe and normal stalk.

Mother's older son (III-2)

The mother's older son is 20 years old. His polyuria is 14 l/day. His diabetes insipidus started when he was 3 years old. The water deprivation test was also compatible with central DI. He has also responded to DDAVP twice daily. Pituitary MRI showed the absence of hyperintense signal in the posterior pituitary lobe and normal stalk.

The father (II-4), 24-year-old daughter (III-3) and 23-year-old daughter (III-4) have never had symptoms of DI and their pituitary MR imaging examinations were normal.

All affected and unaffected members of the family had normal anterior pituitary function (either basal or after specific stimuli).

MR study

Magnetic resonance imaging was performed on a 1.5-T superconductive magnet (Magnetom, Siemens, Erlangen, Germany) using spin-echo (SE) T1-weighted images (TR 500 ms, TE 15 ms, two acquisitions). Sagittal and coronal 3-mm sections with a matrix size of 256×256 pixels and a field of view of 23 cm were obtained. T1-weighted images were also obtained after IV Gd-DTPA (Magnevist, Schering, Berlin, Germany) administration (0.2 ml/kg) in all patients with idiopathic central DI, control subjects and six members of the family (II-3, II-4, III-2, III-3, III-4 and III-5).

Magnetic resonance imaging of a member of the family (III-1) with autosomal dominant DI was obtained by a 0.5-T superconductive magnet (Signa, General Electric, Milwaukee, Wis.) using SE T1-weighted images (TR 200 ms, TE 20 ms, one acquisition). Sagittal and coronal 3-mm sections with a matrix size of 160×192 pixels and a field of view of 25 cm were obtained.

Magnetic resonance imaging of the posterior pituitary lobe and stalk was also performed on 20 control subjects without evidence of polyuria and polydipsia who were being investigated because of secondary hypogonadism or short stature.

Results

Results of MR examinations in patients with idiopathic central DI are summarized in Table 1. All control subjects had normal hyperintense signal on their posterior pituitary MR imaging. All patients with idiopathic central DI lacked the hyperintense signal in the posterior pituitary lobe, but with a normal stalk (Fig. 2).

Affected members of the family with central DI also had absent hyperintense signal with normal stalk in their posterior pituitary MR imaging. However, unaffected members had normal hyperintense signal in their posterior pituitary (Fig. 3). Furthermore, three expert radiologists have evaluated MR imagings from all patients by blinded reading. They have found the same results.

Discussion

The major finding of this study is that all patients with idiopathic central DI and affected patients with familial autosomal dominant DI had the absent hyperintense signal in their posterior pituitary MR imaging. Moreover, unaffected members of the family and control subjects had characteristic high intensity in the posterior pituitary lobe, indicating the usefulness of the MR imaging for evaluation of the functional status of the hypothalamic–neurohypophyseal axis.

That the hyperintense signal was absent in all patients with idiopathic central DI is in agreement with previous reports [5, 6, 13, 17, 18]. In contrast, Maghnie et al. [8] and Cacciari et al. [9] reported normal hyperintense signal in patients with rare idiopathic central DI. These conflicting results may originate from heterogeneity of the group of patients with idiopathic DI [19]. Stanhope et al. [20], supporting this view, reported that two cases of idiopathic DI presented with germinoma 6 and 21 years later. Other possible explanations for the presence of hyperintense signal in patients with rare idiopathic DI may be due to impairment of AVP release or secondary to shortcomings or misinterpretation in the imaging techniques [19].

In normal subjects the frequency of the bright signal has varied from 90 to 100% [13, 18] to as low as 63% [21]. The source of the hyperintense MR signal in the normal neurohypophysis is not clear, but some studies suggest that it may originate from neurosecretory granules and/or the intracellular lipid droplets in the posterior pituitary cells [12–15].

Little is known about MR imaging in familial central DI. To our knowledge, MR imaging has been evaluated in only three families with autosomal dominant DI [7,8,11]. In our family all affected members had the absent hyperintense signal, whereas unaffected members had normal hyperintense signal indicating the usefulness of MR imaging for evaluation of the functional status of the hypothalamic–neurohypophyseal axis. Absent signal could mean the lack of neurosecretory granules in the posterior pituitary lobe or the amount of granules produced was too small to be stored [12, 13, 22]. In agreement with our study, Rutishauser et al. [7] also found absent hyperintense signal in all affected members of a family with autosomal dominant neurohypophyseal DI. In contrast, Miyamoto et al. [11] reported the presence of the bright spot in two of five adult patients with familial central DI, as did Maghnie et al. [8] in two children with autosomal dominant DI. The discrepancy in the studies with familial DI is not clear. It may be related to underlying different genetic defects in these families. The presence of normal bright signal in some patients with familial DI suggests that these patients are able to synthesize and store some amount of AVP in the posterior pituitary, but not necessarily to release it normally. Another explanation is that the accumulated mutant AVP:NP-II complex causes the persistent posterior pituitary bright signal [2]. It is possible that the impaired local proteolytic degradation due to underlying genetic defects or other unknown reasons may result in persistence of the bright spot in these patients. Based on the results from our own findings and previous studies [7,14], we suggest the absence of neurovesicles as the cause of the lack of T1 signal in affected members of our family with autosomal dominant DI.

We conclude that MR can be used to evaluate the functional status of the hypothalamic–neurohypophyseal axis in idiopathic central DI and in familial autosomal–dominant hypothalamic DI. However, the standard method of diagnosing central DI is still based on water deprivation followed by administration of 1-desamino-8–9 arginine vasopressin (DDAVP) as well as by assessment of the renal response to hypertonic saline infusion.

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Book review

European Radiology

Taveras, J.M.: Neuroradiology, 3rd edn. Baltimore: Williams & Wilkins, 1996. 1190 pp., 647 figs., (ISBN 0-683-08112-8), £ 173.00

Juan Taveras is one of the greats of American neuroradiology. He is Emeritus Professor and the former Radiologist in Chief of the Massachusetts General Hospital, as well as a past president of the American Society. This work is the third edition of his text *Diagnostic Neuroradiology,* the title being changed due to the inclusion of a section on interventional neuroradiology, by Dr. J. Pile-Spellman. This section aside, the entire work is written by Dr. Taveras. Since it comprises 1190 pages and 647 illustrations, it certainly represents a magnum opus, and will presumably be the last edition of the book to be wholly written by Dr. Taveras.

Impressed as one must be by the virtuosity of this work, teaching through the medium of a textbook is an art all to itself, and sadly the organisation and presentation of the book do not reflect the undoubted clinical excellence of the author.

This becomes apparent as one views the contents page. There are 18 chapters: the first three deal with physics, technical considerations and anatomy; the next ten describe intracranial pathology; chapter 14 briefly discusses selection of CT versus MRI and functional neuroimaging; the next two cover the spine and craniovertebral junction; and the last two chapters represent angiography and endovascular therapeutic neuroradiology. There is, however, no subdivision of each chapter: a student searching for a particular topic will find this layout difficult, and need to resort to the index. Indeed the grouping of diseases within each chapter is idiosyncratic. Chapter 4, "General pathological conditions", deals with such diverse conditions as brain calcifications, cerebral oedema, brain herniations and hydrocephalus, as well as myelin and myelination. It does not, however, describe metabolic diseases of white matter, or dysmyelination: these are dealt with in Chapter 5, "Brain congenital abnormalities". It would have been much better to include more detailed information regarding each chapter within the contents page. Unfortunately, the poor index compounds the difficulties engendered by the contents page. I found "posterior cerebral artery" and "calcarine artery" among many items not listed.

Organisation of material within each chapter is also less than ideal. For example Chapter 5 deals mainly with metabolic disorders, which are subdivided in the standard manner, but some syndromes are listed in more than one section: Zellweger syndrome is listed and described under "conditions affecting the white matter" as the prototypical peroxysomal *[sic]* disorder, but is missing from the subsection on peroxisomal diseases, only to appear again in the subsection on mitochondrial disorders with the terse message: "see under 'Conditions affecting white matter'". This is both confusing and frustrating, and I am afraid that the overall organisation of the book greatly detracts from some of the content to such a degree that I would seldom refer to it.

Great clinicians are seldom great physicists, and I found much to argue with in the introductory physics section, as well as some statements which I think are frankly wrong. The section really should have been written by a physicist: there are some of those who write clearly and simply enough for a clinician to understand. In his physics chapter, Dr. Taveras states that to gain a T1-weighted spin echo image, a TR of up to 1 s is acceptable, while a T2-weighted spin echo image can be gained with a TR of only 800 ms! Similarly, a TR of over 2000 ms is recommended for a gradient echo T2-weighted image; this should be even longer for a T1-weighted GRE image. Although Taveras lists GRASS and FISP as steady-state gradient echo techniques, he lists spoiled GRASS and FLASH as non-steady-state sequences. The whole section is so brief as to confound its intentions entirely, and is in any case of questionable relevance in an imaging text when so many excellent small MRI physics books are available.

The other weak sections are to my mind those on angiography and interventional neuroradiology. Unfortunately the illustrations are too small, usually 5 cm × 5 cm, and most are taken from unsubtracted angiograms rather than digital subtraction angiography images. Some of the appended arrows are tiny, and occasionally (as in figure 17.75) they point the wrong way, indicating an area of an image in which no vessel is apparent at all. Similarly the interventional section is far too short for its apparent purpose of describing every possible endovascular technique. Inevitably this leads to anomalies: the Scheglov balloon technique for occluding cerebral aneurysms is described in more detail than the GDC technique, which is allocated only one table and the text words "a microcatheter is navigated into the aneurysm, and the coil is navigated into the vessel".

The bare statement "posterior inferior cerebellar artery aneurysms can be successfully treated by endovascular occlusion of the vertebral artery at C1 level (Hunterian ligation)" should not have been left without explanation, and there is no discussion on which aneurysms are less suited to the GDC technique.

The book does, however, have its strengths. Cerebral and spinal conditions are well described, and the overall coverage of neurological and neurosurgical conditions is certainly comprehensive.

In deciding whether or not to recommend the book, I have also reviewed the most obvious competition: *Diagnostic Neuroradiology* by Anne Osborne (Mosby, St Louis, USA, 1994). I must say that Osborne's book is, in my opinion, far superior: it is better and more logically laid out, has much better illustrations, many in colour; the tables and lists are clear and precise; and an incisive thought process is obvious throughout. For the reader seeking a textbook on modern neuroradiology, I regret that I cannot recommend the volume by Taveras.

S. Halpin, Cardiff